IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of :

Tohru UEDA et al. :

Serial No. [NEW] : **Attn: Application Branch**

Filed September 26, 1995 : **Attorney Docket No. 279-20117RI**

PYRIMIDINE 2'-METHYLIDENE NUCLEOSIDE COMPOUNDS
(Rule 62 Continuation of Serial No. 08/081,183, filed June 25, 1993) :

SECOND SUPPLEMENTAL REISSUE DECLARATION

Undersigned declare:

That with regard to applicants' claiming less than they had a right to claim, the following is a chronology of how and when the error occurred:

As of December 28, 1988, it was confirmed by applicants that the N^4-stearoyl compound (R^1=-$NHCOC_{17}H_{35}$, R^2=R^3=R^4=H, compound of Example 1) was intraperitoneally administered for five consecutive days at a high dose of 100 mg/kg/day to mice (three per group) intraperitoneally implanted with L-1210 leukemia cells and the T/C (%) [(average survival days of drug-administered group/average survival days of the non-administered group) X 100] was calculated. The obtained percentage was 298 and one out of three mice survived not less than 30 days (i.e., the compound being highly active).

Thereafter, on December 7, 1989, a U.S. patent application (hereinafter referred to as the parent application) was filed and a first Office Action issued on June 18, 1990, wherein the parent application was rejected under 35 USC 102(a) over Takenuki et al., Journal of Medicinal Chemistry, vol. 31, No. 6, pp. 1063-1064 (1988) and under 35 USC 112, second paragraph.

In response to the Office Action, applicants deleted "acylamino" as well as several other groups from the definition of R^1 in the claims in the response dated October 18, 1990, despite the fact that the assignee had the data demonstrating the superior antitumor activity at high doses as mentioned above at the time of

filing a response to the Office Action. Accordingly, such deletion was erroneous and unnecessary.

The importance of such data was overlooked by the assignees, partly because its therapeutic route was via intraperitoneal administration, whereas assignees were more interested in oral administration. As a result, the assignees erroneously and unnecessarily agreed to delete from claim 1 terminology which encompasses the compounds in question.

After the grant of the parent application on June 25, 1991, the compounds encompassed in the application were synthesized and developed with the aim of achieving superior antitumor effects against solid tumors by oral administration.

By July 28, 1992, the assignees had determined that it was the compounds wherein R^1 is acylamino having 2 to 30 carbon atoms and $R^2=R^3=R^4=H$, which compounds were initially encompassed by claim 1 of the parent application that actually met said goal, and that for this reason, in addition to the above reason, it was also error to cancel said term "acylamino" by the amendment of October 18, 1990, whereby the desired compounds were no longer encompassed by claim 1.

On March 23, 1993, assignees (Yoshitomi and Yamasa) had a meeting and decided to request the U.S. attorney handling the case, via Takashima International Patent Office (Takashima), assignees' Japanese attorneys, to consider the filing of a reissue.

On April 16, 1993, Takashima requested the U.S. attorney to consider the matter, and on April 22, 1993, the U.S. attorney reported to Takashima concerning the appropriateness of filing of the reissue application.

The present reissue application presents new claim 11 which corresponds to claim 1 of the issued patent, but additionally recites in the definition of R^1 that it represents "acylamino having 2 to 30 carbon atoms" to provide protection for the desired compounds discussed above.

New claim 12 corresponds to original claim 2, but depends on new claim 11 rather than original claim 1.

They further declare that all statements made herein of their own knowledge are true, and that all statements based on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

1st Inventor: Sumiko Ueda — Date: October 24, 1995
Tohru UEDA, Deceased,
by his legal representative,
Sumiko UEDA

2nd Inventor: Takuma Sasaki — Date: November 22, 1995
Takuma SASAKI

3rd Inventor: Akira Matsuda — Date: October 19, 1995
Akira MATSUDA

4th Inventor: Takanori Miyashita — Date: October 16, 1995
Takanori MIYASHITA

5th Inventor: Shinji Sakata — Date: October 16, 1995
Shinji SAKATA

6th Inventor: Keiji Yamagami — Date: November 20, 1995
Keiji YAMAGAMI

7th Inventor: Akihiro Fujii — Date: November 9, 1995
Akihiro FUJII

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re patent of	:	
Tohru UEDA et al.	:	
Patent No. 5,026,835	:	ATTN: APPLICATION BRANCH
Issued June 25, 1991	:	
PYRIMIDINE 2'-METHYLIDENE NUCLEOSIDE COMPOUNDS	:	

CONSENT OF ASSIGNEE TO FILING OF REISSUE APPLICATION

Honorable Commissioner of Patents and Trademarks,
Washington, D.C.

Sir:

Yamasa Shoyu Co., Ltd. (now Yamasa Corporation as a result of a corporate name change) and Yoshitomi Pharmaceutical Industries, Ltd., co-Assignees of the entire interest in the subject patent, by virtue of an Assignment recorded on February 5, 1990 at Reel 5231, Frames 204 to 205, hereby consent to the filing of the attached Reissue application.

The undersigned have reviewed all the evidentiary documents in the chain of Title of the above patent and, to the best of the undersigneds' knowledge and belief, title is in the Assignees indicated above.

The undersigned verify that they are authorized to take this action on behalf of Yamasa Corporation and Yoshitomi Pharmaceutical Industries, Ltd.

The undersigned hereby declare that all statements made herein of their own knowledge are true, and that all statements made on information and belief are believed to be true; and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements

may jeopardize the validity of the application or any patent issuing thereon.

October 25, 1995
Date

Michio Hamaguchi
Name Michio Hamaguchi Title President
Authorized Signing Officer
of Yamasa Corporation

December 5, 1995
Date

Masashi Goya
Name Masashi Goya Title President
Authorized Signing Officer
of Yoshitomi Pharmaceutical
Industries, Ltd.